Question Bank

PHARMACOTHERAPY

Study Design

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1. **Q.1**: Four new drugs have been compared with placebo to determine their ability to prevent a first myocardial infarction (MI) in men with high low-density lipoprotein cholesterol (LDL-C). After a median follow-up of 5 years, the following was observed:
   i. Drug A reduced the rate of first MI by 30%.
   ii. Drug B resulted in an absolute reduction in deaths of 2.4%.
   iii. Drug C showed that 42 men are needed to undergo treatment to prevent a single first MI.
   iv. Drug D reduced first MI from 7.9% of patients (placebo group) to 5.5% of patients (drug D group) at 5 years. **©**

   Answer:

2. **Q.2**: Questions 1 and 2 pertain to the following case narrative. A recently released statin is associated with less myopathy than other currently available statins. After 2 years of use, a retrospective case-control study was undertaken by the manufacturer after 20 different reports of severe myopathy were sent to the U.S. Food and Drug Administration's (FDA) Med Watch program. Risk factors for statin-induced myopathy were not assessed; however, both the cases and the controls of this study had identical diagnostic evaluations and were stratified according to the duration of statin use before the onset of myopathy.

1) Which type of bias is this study design most susceptible to?

A. Confounding by indication.
B. Recall bias.
C. Diagnostic bias.
D. Misclassification.

2) Which factor will be most affected by the type of bias likely to occur in this study?

A. External validity.
B. Internal validity.
C. Assessment of exposure.
D. Number of patients needed for the study.

Answer :

1- B

Comment: Recall bias is always a potential concern for case control studies because of the amount of time that passes between the study and the drug "ingestion." Because risk factors were not included in the study design, this is of concern. Although a study may be susceptible to many types of bias, the other choices would not pose as much risk (if any) compared with recall bias.

2- B

Comment: Internal validity is greatly jeopardized because the study is not designed to protect against this possible bias. In a sense, this design flaw jeopardizes external validity (how well does a study apply to other patients with this condition/disease?), but a lack of internal validity is most affected. The other answers can be adequately controlled for in the design and conduct of the study.

3. **Q.3:** When describing the results of a randomized controlled clinical trial, the investigators report using an intention-to-treat analysis to analyze their data. The results of their investigation comparing two diuretics for heart failure show no difference in the number of hospitalizations for decompensated heart failure between the treatment groups. Given their method of data analysis, which statement is most appropriate?
   A. May be susceptible to issues regarding a lack of power.
   B. Provides a good measure of effectiveness under typical clinical conditions.
   C. Cannot provide an estimate of the method's effectiveness.
   D. May overestimate the actual treatment effect.

Anwer: B

➢ **Comments** :

- Intention-to-treat analysis generally considers the approach, which gives the best estimate of use effectiveness (use under typical clinical-trial conditions), whereas per-protocol analysis gives a better estimate of method effectiveness (use under ideal conditions)
- **(Answer B is correct, and Answer C is incorrect).**
  Intention-to-treat analysis is the most common approach to data analysis for randomized controlled trials and may underestimate the treatment effect **(Answer D is incorrect)**.
- A per-protocol analysis discards data from patients who do not adhere to the treatment to which they were initially randomized; hence, it is susceptible to a loss of power to detect differences between groups.
- This loss of power occurs as patients are removed from the analysis completely because of no adherence, which decreases the sample size of the study and thus the power to detect differences.

4. **Q.4:** A prospective randomized study compared once daily enoxaparin with twice-daily enoxaparin when treating patients with venous thromboembolism (VTE). One of the study end points was the recurrence of VTE. The following table summarizes recurrence rates in all patients. Once Daily Twice Daily All patients – n (%) 13/298 (4.4) 9/312 (2.9) The 95% confidence interval (CI) for the difference in recurrence rates between the two groups was -1.5% to 4.5%. Which conclusion is most appropriate?

A. The difference in recurrence rates between the two treatments is statistically significant.

B. The difference in recurrence rates between the two treatments is not statistically significant.

C. Because twice-daily therapy causes fewer recurrences, clinicians should feel comfortable using that dosing scheme for their patients with VTE.

D. No conclusion can be drawn because p-values are unavailable.

Answer: B

- **Comments:**
  - The CI of the difference in recurrence rate between the two groups includes zero; thus, there is no statistically significant difference between the two groups.
  - **Answer A is incorrect** because the 95% CI contains zero and therefore is not statistically significant.
  - **Answer C is incorrect** because twice-daily therapy did not have fewer recurrences. Because of the lack of statistical significance, it is unreasonable to conclude that twice daily therapy would be more appropriate in this or any other patient population.
  - **Answer D is incorrect** because all the above information can be determined without the benefit of reported p-values.

5. **Q.5:** According to the data in the previous question and the result obtained, which best represents the number of patients who would need to be treated with twice-daily enoxaparin to prevent the recurrence of one VTE?
   A. 7.
   B. 23.
   C. 67.
   D. Number needed to treat (NNT) should not be calculated because the result was non-significant.

   Answer: D

   - **Comment:**
     - The first two answers are incorrect calculations.
     - Calculating the NNT to prevent one recurrence using twice-daily therapy is as follows: 0.044 − 0.029 = 0.015 and 1/0.015 = 66.7…67.
     - Answer D is correct because the NNT should not be calculated when the end point of interest is non-significant.

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6. **Q.6** In a study of 26000 females, 1300 subjects were found to have either overt or subclinical hypothyroidism. Within this group, the risk of demonstrating either overt or subclinical hypothyroidism was therefore 5%.

   What is the best descriptive term of this 5% risk?

   Available marks are shown in brackets
   1) Absolute risk]
   2) Incidence]
   3) Prevalence
   4) Relative risk]
   5) Specificity]

Answer 3:

- **Comment**: This is the risk of either subclinical or overt hypothyroidism in a female population at any specific time which is the prevalence.
  This is defined as the rate of a disorder in a specified population at a specified time. Incidence refers to the number of new cases of a disorder developing over a specific time.

7. **Q.7**: Questions 6 and 7 pertain to the following case narrative. A multicenter, double-blind, placebo-controlled trial randomly assigned 4837 patients to treatment with margarine supplemented with the omega-3 fatty acid ALA (margarine with ALA) or a placebo margarine. The primary combined end point was the rate of cardiovascular events, defined as fatal and nonfatal cardiovascular events and percutaneous coronary interventions. Data were analyzed according to intention-to-treat analysis with the use of a Cox proportional hazards model. The 95% hazard ratio (HR) and 95% CI for the margarine with ALA group were 0.91 and 0.78–1.05. In the pre-specified subgroup of women, margarine with ALA was associated with an HR of 0.73 (95% CI, 0.51–1.03).

6) Which statement is most appropriate?

A. Margarine with ALA statistically significantly reduced the risk of cardiovascular events ($p<0.05$).
B. Margarine with ALA statistically significantly reduced the risk of cardiovascular events ($p<0.01$).
C. Margarine with ALA did not significantly reduce the risk of cardiovascular events ($p>0.05$).
D. Without a p-value, it is not possible to determine whether margarine with ALA affected cardiovascular events.

7) When the study was being designed, which choice describes the outcome for which the study was most likely to have been powered?

A. Differences in the rate of the composite outcome, cardiovascular events.
B. Differences in the rate of percutaneous coronary interventions.
C. Differences in the rate of the composite outcome in women.
D. Differences in the rate of the composite outcome in men.

Answer: 6. C

- Comment:
  - **Answer A and Answer B are incorrect** because the margarine with ALA did not significantly reduce the risk of cardiovascular events (the 95% CI includes 1 [no difference in risk]).
  - **Answer D is incorrect** because the p-value is not required for interpreting statistical significance, when the 95% CI is provided.
  - **In Answer C**, the p-value corresponds to the 95% CI.

Answer: 7.A

- **Comment:** Clinical trials are usually adequately powered to compare primary end points. Because Answer B is part of the composite outcomes, the study was likely not powered to detect this outcome independently. Similarly, even though the subgroup analysis was determined a priori, the study is not typically designed to have sufficient power to make this comparison.

8. **Q.8**:In a meta-analysis of randomized controlled trials examining the effects of several antihypertensive drugs, the odds ratio (OR) for treatment with low-dose diuretics compared with calcium channel blockers for cardiovascular disease events was 0.84 (95% CI, 0.75–0.95).

Which statement is the most appropriate interpretation of these findings?

A. Treatment of hypertension with low-dose diuretics was more effective in preventing cardiovascular disease events than treatment with calcium channel blockers.

B. Treatment of hypertension with calcium channel blockers was more effective in preventing cardiovascular disease events than treatment with low doses of diuretics.

C. The difference observed between treatment with calcium channel blockers and low doses of diuretics is not statistically significant.

D. The odds of a patient developing cardiovascular events when treating hypertension with low doses of diuretics are lower than when using calcium channel blockers.

Answer: D

- Comment:
  - **Answer A and B are incorrect** because each implies that one drug is more effective than the other.
  - In this type of study design, neither drug is more/less effective.
  - **Answer C is incorrect** because the CI of the OR does not include 1; thus, the finding is statistically significant at the 5% level.

9. **Q.9**: A clinical trial assessing a new lipid lowering therapy for stroke allocates 1000 patients to active treatment and another 1000 patients to placebo. Results demonstrate that number needed to treat (NNT) is 20 for the prevention of the primary end-point. Which of the following best describes the results?

   Available marks are shown in brackets
   1) 20 patients in the treatment group were protected from stroke. [0]
   2) 20 extra patients in the placebo group had a stroke
   3) For 1000 patients treated with active therapy, there would be 20 fewer strokes [
   4) For 1000 patients treated with active therapy, there would be 50 fewer strokes.
   5) For every 1000 patients treated with active therapy there would be 100 fewer strokes

   Answer 4:

   - **Comments**: This prevention study for stroke reveals that 20 patients need to be treated to prevent one event. Thus if you treat a 1000 patients then you will expect to have 50 fewer strokes.

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10. **Q.10**: A publication reports the outcome of a new statin therapy in a placebo controlled primary prevention of ischemic heart disease in a diabetic population. 1000 patients were randomized to receive the new therapy and 1000 allocated to placebo. The study was completed over a five year period. In the placebo group there were 150 myocardial infarcts and in the group treated with the new statin there were 100 infarcts. What is the relative risk reduction of MI afforded by statin therapy?

    Available marks are shown in brackets
    1) 15%
    2) 25%
    3) 33%
    4) 40%
    5) 50%

    Answer 3:

    - Comments:
      - There are 50 fewer MIs in the treated group then the placebo treated group, hence 50/150=33%.
      - The relative risk reduction provides information regarding the efficacy of a therapy and what reduction in risk may be expected when treating subjects rather than just having data relating to the significance of the data.

11. Q.11: A study comparing contrast CT colonography with the reference technique of colonoscopy for large bowel carcinoma reveals the following data in 400 patients: Investigation CT Positive CT Negative Colonoscopy Positive 30-10 Colonoscopy negative 20-340.Which one of the following most accurately describes the performance of CT versus colonoscopy for the diagnosis of large bowel cancer?

Available marks are shown in brackets

1) There are 340 false negatives
2) There are 370 false negatives
3) There are 10 false positives
4) There are 20 false positives
5) There are 20 true negatives

Answer 4

- **Comments:**
  - There are 40 true positive patients identified by Colonoscopy with colon cancer and 10 of these are false negatives as identified by CT. There are 360 patients without the disease with 20 identified as having cancer with CT (false positives).

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12. Q.12: A study reports on the results of a large study of the primary prevention of stroke in a diabetic population using a new antiplatelet agent versus aspirin. The results of the study reveal that over a 5 year period the incidence of stroke in the aspirin treated group is 3% compared to a rate of 1.5% in the group treated with the new antiplatelet agent ($p<0.001$). What is the relative risk reduction in stroke associated with the new drug? Available marks are shown in brackets

1) 1.5% [0] 2) 15% [0] 3) 30% [0]
4) 40% [0] 5) 50% [0]

Answer 5:

- **Comments:**
  - The relative risk reduction is another calculation important for the interpretation of publications. In this case there is an absolute risk reduction of 1.5% (3 - 1.5%) in stroke afforded by the new agent compared with aspirin yet the relative risk reduction is 1.5/3=50%.
  - That is 50% fewer strokes may be prevented by the use of the newer agent compared with aspirin, although this would be the equivalent of 15 per 1000 patients treated (30 strokes expected/1000 patients treated with aspirin but only 15 with the new drug).

13. Q.13.A new diagnostic test for malabsorption has been analyzed and the results have yielded the following 2x2 contingency table. Disease present test result yes no +ve 0.9 0.1 & -ve 0.2 0.8 Applying this test to a case of chronic diarrhea from a patient group where the prevalence of malabsorption is known to be 20% (probability = 0.2) what is the probability of a patient having malabsorption if they have a positive test?

Available marks are shown in brackets

1) 0.16 [0]
2) 0.24 [0]
3) 0.48 [0]
4) 0.64 [0]
5) 0.8 [0]

Answer 4

- Comments:
  - This is tough but the College are putting more and more Evidence Based Medicine Questions into the exam.
  - This question tests understanding of pre-test and post-test odds, likelihood ratios, sensitivity and specificity. The calculation is as follows.
    Sensitivity = 0.9/(0.9 + 0.2) = 0.818
    Specificity = 0.8 / (0.1 + 0.8) = 0.889
    Likelihood ratio for a postivie test (LR+) = 0.818 / (1 - 0.889) = 7.2
    Pre-test odds = 0.2 / (1 - 0.2) = 0.25
    Post-test odds = pre-test odds X LR+ = 0.25 X 7.2 = 1.8
    Post-test probability = 1.8 / (1.8 + 1) = 0.64

14. **Q.14**.A paper describes a new diagnostic test for myocardial infarction. You want to know what proportion of patients who are classified as not having had a myocardial infarction by the test will actually not have had a myocardial infarction. Which one of the following measurements would indicate this? Available marks are shown in brackets

1) accuracy [0]
2) negative predictive value [0]
3) positive predictive value [0]
4) sensitivity [0]
5) specificity [0]

Answer 2

- Comments:
  - The proportion of **'true negatives'** not having had a MI correctly identified by this test is called **the Negative predictive value** and refers to the number accurately identified to not have MI by the new test over the number without MI identified by the test + those wrongly identified as not having had an MI.
  - **Specificity** is the number without MI accurately predicted.
  - **Sensitivity** refers to the number correctly identified with MI by the new test.
  - **A positive predictive value** refers to the number accurately identified with MI by the test over the number accurately identified with MI + those wrongly identified with MI.

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15. **Q.15**: A publication reports the outcome of a new statin therapy in a placebo controlled primary prevention of ischemic heart disease in a diabetic population. 1000 patients were randomized to receive the new therapy and 1000 allocated to placebo. The study was completed over a five year period. In the placebo group there were 150 myocardial infarcts and in the group treated with the new statin there were 100 myocardial infarcts. What is the number needed to treat to prevent one MI over the course of this study?

Available marks are shown in brackets

1) 10 2) 20 3) 30 4) 40 5) 50

Answer 2

- **Comments:**
  - You treat 1000 patients for 5 years with the new statin and prevent 50 MIs.
  - Thus the Number Needed to Treat (NNT) to prevent 1 MI is 20 (1000/50).
  - Again, this statistical figure provides us with a lot of information regarding the efficacy of a treatment rather than purely statistically significant data.
  - As it stands, you may expect to prevent an infarct by treating as few as 20 patients over 5 years from this data.
  - Furthermore, cost economic data can be calculated from such results by factoring in how much the drug costs against all the costs of treating and rehabilitating a patient with an MI.

16.Q.16: Statistical independence may be assumed in which of the following circumstances?

Available marks are shown in brackets:

1) Successive measures taken on the same individual. [0]
2) Stratified sampling from a target population. [0]
3) Two matched individuals in a case control study. [0]
4) Response to antibiotics of children with otitis media who have a CRP of above 100. [0]
5) Diagnosis of pyloric stenosis by ultrasound scan in patients attending a tertiary referral center. [0]

Answer 2

- **Comments:**
  - Independent events do not affect each other. Thus, the chance of event A occurring is completely unaffected by the chance of B occurring.
  - Two measures on the same individual are clearly dependent, but the same also applies to 2 matched individuals such as in a case control study.
  - The outcome of patients attending a tertiary referral center is bound to depend on the patients referred, and the facilities and expertise available at that center.
  - In patients with elevated CRP, one might suspect that there is a higher risk of bacterial otitis media, and, therefore, one might expect a greater response to antibiotics. The response to antibiotics is, therefore, dependent to some extent on the raised CRP.

17.Q.17:A study of a new chemotherapy drug for lung cancer is reported in a medical journal. The authors state that with the new agent the 5-year mortality rate was 60%. Without treatment the 5-year mortality rate was 80%. Which of the following represents the Absolute Risk Reduction using this treatment? Available marks are shown in brackets

1) 10% [0] 2) 20% [0] 3) 25% [0] 4) 33% [0] 5) 40% [0]

Answer 2

- Comments:
  - The absolute risk reduction is an important figure and should always be quoted instead of the the relative risk reduction.
  - Examples. If a drug reduces the incidence of heart attacks from 10% to 5% then ...
    - the control event rate (CER) is 10%
    - the experimental event rate (EER) is 5%
    - the relative risk reduction (RRR) is 50%
    - the absolute risk reduction (ARR) is 5%
    - the number needed to treat (NNT) is 100% / 5% = 20

18. Q.18:A study has been designed to investigate whether a certain drug plus physiotherapy treatment is better than drug treatment alone in the management of rheumatoid arthritis. After randomizing the patients a small proportion of the drug plus physiotherapy group decide to drop out of the study or omit some treatment sessions specified in the research protocol. What is the correct way of analyzing the subsequent data? Available marks are shown in brackets

1) Assume the patients have withdrawn their consent [0]
2) Exclude these patients from all analysis [0]
3) Extend the trial recruitment to make up the numbers [0]
4) Include these patient outcomes in the drug plus physiotherapy group [0]
5) Interview the patients and report their group separately [0]

Answer 4

- **Comments:**
  - This is the principle of 'intention to treat'. It is possible that the physiotherapy intervention was harmful to the patients and this is why they left.
  - Intention to treat helps to reduce bias by sticking to the original allocation of treatment and analyzing the patient in that treatment group even (and concentrate for this bit) even if they don't get it!

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19. Q.19: In a study of elderly patients with atrial fibrillation, patients receiving warfarin (n= 6000), 6% had strokes or died as a consequence of stroke, whereas in subjects treated with aspirin (n = 8000), 9 % had stroke or death from a stroke over the 3 year study period (p=0.001). The risk of stroke in an untreated population with atrial fibrillation over this time was 12%. Which of the following percentages is the approximate annual incidence of stroke in the treated population in this study? Available marks are shown in brackets

1) 2.6% [0] 2) 3.3% [0] 3) 5.5% [0] 4) 6.9% [0] 5) 7.7% [0]

Answer 1

- Comment:
  - One needs to calculate the incidence as follows: In the group treated with warfarin there were 360 strokes (6% of 6000).
  - In the aspirin treated group there were 720 strokes (9% of 8000).
  - Thus, there are 1080 strokes amongst the treated population (n=14000) over a three year time period. Therefore there are 360 strokes annually in the treated group (14000) giving an annual incidence of stroke of approx 2.6%

    Note: remember to divide by three since the study lasted 3 years and the figures given are for the 3 years incidence rates.

20. Q.20: In a trial of statin therapy in the secondary prevention of ischemic heart disease, therapy is shown to reduce cardiovascular mortality from 12% to 8% over the 5 years duration of the study. In comparison with standard therapy, what is the number of patients that need to be treated to prevent one death over five years? Available marks are shown in brackets

1) 5 [0] 2) 10 [0] 3) 20 [0]

4) 25 [0] 5) 50 [0]

Answer 4

- **Comments:**
  - The drug has reduced the risk of death post MI by 4% over 5 years.
  - Therefore if 100 people were treated we could expect the prevention of 4 deaths. Therefore in order to prevent 1 death, 25 individuals would need to treat.

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21. Q.21: In a study assessing two different antiplatelet agents in the prevention of stroke, 10,000 subjects were randomized to receive either the standard therapy or the new therapy. Over the study period of five years, the side effect of major gastrointestinal bleeding was 3% in the standard therapy group compared with 2% in the new therapy group. Which of the following is the absolute risk reduction associated with the new therapy in major GI bleeds? Available marks are shown in brackets

1) 1% [0] 2) 3% [0] 3) 10% [0]

4) 15% [0] 5) 33% [0]

Answer 1

- **Comments:**
  - We are not told whether there is a significant difference between the two groups yet in the standard antiplatelet therapy group there is a risk of GI bleed of 3% vs 2% with the new therapy.
  - This is a 1% absolute risk reduction and a 33% relative risk reduction (1/3).
  - The number of people that would need to be treated with the new drug to avert the major effect of bleeding would be 100.

22.Q.22:Adequate randomization can be assumed in which of the following circumstances? Available marks are shown in brackets

1) All consecutive patients attending a tertiary referral center.

2) A sample using healthy volunteers. [0]

3) A sample of those judged to be appropriate for inclusion in the study.

4) A sample based on a family cluster. [0]

5) A stratified random sample. [0]

Answer 5

- **Comment:**
  - The actual patients included in the study often differ substantially from what was initially intended. This dramatically alters one's interpretation of a study. The target population includes all those with a given disease, and is seldom fully accessible.
  - The accessible population available for study may be biased in time or place. It is important to randomize when selecting a sample which are supposed to represent the target population.
  - In simple randomization, every member of the population is numbered, and a random sample is selected.
  - In a stratified random sample, groups of interest are identified, and then randomization occurs within those groups. In systematic sampling a "periodic" approach is used. This is not really random and is open to alteration and bias.
  - In a cluster sample, a natural grouping of population is used (such as a family), but this may well be unrepresentative of the whole population.

    Classic errors in randomization are:

    • Consecutive sampling, which may well not be representative if the study time is short.

    • Convenience sampling: strong potential for bias, with volunteers generally healthier than others.

    • Judgmental sample: including those that you want only. The potential for systematic error is enormous

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23. **Q.23**:In a study of 950 subjects with a BMI below 25, a new serological marker for coeliac disease was assessed against the gold standard test of jejunal biopsy. The following results were obtained: Test positive Test negative: Biopsy positive 40-10, Biopsy negative 60-840 What is the sensitivity of this test? Available marks are shown in brackets

1) 40% [0] 2) 55% [0] 3) 66% [0] 4) 80% [0] 5) 93% [0]

Answer 4

- **Comments:**
  - Sensitivity relates to the probability that the person with a disease will be correctly identified with the disease.
  - Therefore, in this study, 50 subjects have the disease, of whom 40 are correctly identified with the disease giving a sensitivity of 80%(40/50).
  - The specificity is the probability that a person without the disease will be correctly identified by the test.
  - In this case, there are 900 subjects without the disease of whom 840 were identified by the test – giving a specificity of 93%(840/900)

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24. **Q.24:** A study was performed to assess the usefulness of a new autoantibody test for the detection of suspected Hashimoto's disease. The test was undertaken in 1000 subjects who complained of tiredness and all test results were compared with FNA biopsy results which provided a gold standard for the diagnosis of Hashimoto's disease. The following table lists the results: Antibody +ve Antibody -ve Total Hashimoto's disease confirmed at FNA 35-15-50 No evidence of disease at FNA 30 - 920- 950 Approximately, what is the sensitivity of the antibody test for the detection of Hashimoto's disease?

1) 50% [0] 2) 60% [0] 3) 70% [0] 4) 80% [0] 5) 90% [0]

Answer 3

- Comment:
  - The Sensitivity of a test is the ability of a test to identify those with the condition. In this example, 50 individuals had Hashimoto's disease according to the Gold standard test of biopsy, with 35 of these being identified by the antibody test. 35/50x100 =70%.

25. Q.25: A randomized double-blind placebo controlled study of a cholesterol-lowering drug for the primary prevention of coronary heart disease was conducted. It had a five-year follow up period. The results showed an absolute risk of myocardial infarction in the group-receiving placebo during was 10 per cent. The relative risk reduction of those given the cholesterol lowering medication was 0.8. Approximately what number of patients will need to be treated with the drug for five years to prevent one myocardial infarction?
Available marks are shown in brackets

1) 10 [0] 2) 13 [0] 3) 15 [0] 4) 20 [0] 5) 23 [0]

Answer 2

- **Comment:**
  - This is a question concerning Number Needed to Treat (NNT).
  - The calculation involves a little arithmetic.
  - The absolute risk of MI in the group is a pretty high 10%
    (i.e: of 1000 patients on placebo 100 will have MI over 5 years).
  - The relative risk reduction is stated as 0.8 (i.e 80%).
  - Therefore, if you treat 1000 patients for 5 years with the cholesterol lowering agent you'll get only 20 MIs.
  - Thus, for 1000 patients treated you'll get 80 fewer MIs. Thus Number Needed to Treat to get 1 fewer MI is 1000/80 = 12.5.
  - Or, if you're any good at remembering formulae you can remember the following: -
    1- Relative risk reduction (RRR) = Absolute risk reduction (ARR) / Control event rate (CER).
    2- Numbers needed to treat (NNT) = 1 / Absolute risk reduction (ARR) You can then just insert the figures into these formulae.
  - The control (or placebo) event rate (CER) is 10% or 0.10. The relative risk reduction is 0.80. Inserting these figures into the above formulae … .
    RRR = ARR / CER 0.80 = ARR / 0.10 ARR = 0.80 * 0.10 = 0.08
    Then the NNT can be calculated by NNT = 1 / ARR = 1 / 0.08 = 12.5.
  - **However**, if algebra isn't your thing you could try working with real numbers. Imagine a group of 100 patients (it makes the maths easier).
  - In the control (or placebo group) 10% (or 10 patients) suffered an MI. The relative risk reduction is 0.8 or 80%. Therefore, in the treatment group, there would be a reduction in events by 80% (of 10 patients) = 8 patients. The number of patients suffering an MI in the treatment would therefore be: 10 – 8 = 2 patients. It can therefore be said that treating 100 patients with the new drug would result in 8 fewer MIs.
  - The number needed to treat to prevent one MI would be 100/8 = 12.5 patients.

26. Q.26: In a study of elderly patients with atrial fibrillation, patients receiving warfarin (n= 6000)were found to have a rate of stroke of 6% whereas subjects treated with aspirin (n = 8000)had a stroke rate of 9.9% over the 3 year study period (p=0.001). The risk of stroke in an untreated population with atrial fibrillation over this time was 12%. To what do these numbers relate? Available marks are shown in brackets

1) Absolute risk [0] 2) Incidence [0] 3) Odds risk [0]

4) Prevalence [0] 5) Relative risk [0]

Answer 2

- **Comments:**
  - These numbers relate to the INCIDENCE of stroke occurring in various populations over a specified period of time. Prevalence is the numbers of patients with a specified disorder at any one time point. Absolute risk reduction refers to the reduction in the number of patients with stroke following a specific intervention e.g ARR of stroke with warfarin vs aspirin is 3.3% over 3 years. Relative risk reduction is 3.3/9.9x100 = 33%.

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27. Q.27:A researcher is trying to design a study to find out the cause (or causes) of a rare disease, about which very little is known. What study design is most likely to be appropriate?

A : Geographical B : Cross-sectional C : Cohort

D : Intervention E : Case control (**Answer D)**

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28. Q.28: A letter to a medical journal suggested that an established antidepressant may cause photosensitivity. The manufacturer wished to set up a study to determine rapidly and efficiently whether this was a true association. Which one of the following techniques is most appropriate? Available marks are shown in brackets

1) A case control study [0]

2) A dose ranging study [0]

3) A double blind, randomized, placebo controlled study [0]

4) A meta-analysis [0]

5) A sequential trial [0]

Answer 4

- Comments:
  - **A sequential trial** is one in which the data are analyzed after each participant's results become available, and the trial continues until a clear benefit is seen in one of the comparison groups, or it is unlikely that any difference will emerge. The main advantage of sequential trials is that they will be shorter than fixed length trials when there is a large difference in the effectiveness of the interventions being compared. Their use is restricted to conditions where the outcome of interest is known relatively quickly.
  - **In a case control study**, patients who have developed a disease are identified and their past exposure to etiological factors is compared with that of controls who do not have the disease.
  - **A double-blind randomized** placebo controlled study does not seem appropriate in this case, and a dose-ranging study would be used in the early stages of drug development to identify common side effects, perhaps toxicity, and threshold efficacy doses.
  - The most appropriate study would probably be a meta-analysis. This is because the drug is in the market place, large studies will have taken place in order for it to obtain its license, the data is available relatively rapidly (compared with the other options in this question), the analysis could be carried out efficiently (cheaply if one were being cynical), and the results of the trial would also be available rapidly.

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29. Q.29: A new treatment for osteoarthritis has been developed and shown to be effective in animal models plus its effects in small numbers of patients appears promising. However, there are some concerns with regard to possible hepatoxicity but no cases have been observed in studies thus far. Which is the most appropriate next step in this drug's development? Available marks are shown in brackets

1) case control study [0]

2) double blind randomized placebo controlled study [0]

3) Drug development should be suspended due to the hepatoxicity [0]

4) open label study [0]

5) single blind randomized placebo controlled study [0]

Answer 2

- Comments:
  - This drug has completed animal trials and has been tested in human volunteers (phase 1) and has also been tried in patients (phase 2). Thus the next stage in its development is a phase 3 study and the best phase 3 study would be a randomized control study.

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30. Q.30: A publication assesses a new diagnostic test for thyroid cancer. Which of the following terms would reflect the number of cases of thyroid cancer correctly identified by this new test? Available marks are shown in brackets

1) accuracy [0] 2) negative predictive value [0]

3) positive predictive value [0] 4) Sensitivity [0] 5) Specificity [0]

Answer 4

- **Comments:**
  - The specificity of a test is the probability that a test will produce a true negative result when used on an unaffected population, whereas the sensitivity of a test is the probability that it will produce a true positive result when used on an affected population (as determined by a reference or "gold standard").
  - The positive predictive value of a test is the probability that a person is affected when a positive test result is observed. The negative predictive value of a test is the probability that a person is not affected when a negative test result is observed.
  - Accuracy is expressed through the above four parameters.

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31. In a double blind controlled trial assessing the impact of a new antihypertensive in the treatment of stroke versus conventional antihypertensive therapy in the secondary prevention of stroke, the authors report an absolute annual risk reduction in the incidence of stroke of 0.5% and a relative risk reduction of 20%(p=0.032). The cost of the new treatment is £100 more expensive per year than conventional therapy. What would be the cost of implementing the new therapy for each stroke prevented?

Available marks are shown in brackets

1) £2000 2) £4000 3) £10,000 4) £20,000 5) £50,000

answer 4

Comments:

In this case, the annual incidence of stroke is reduced by 0.5% and treatment is £100 more than conventional therapy. The relative risk reduction of 20% means that the annual risk of stroke is 2.5% (0.5% is 1/5 of 2.5%) in the conventionally treated group. Thus for every 200 patients treated 1 less stroke would occur with the new drug versus the conventional therapy. Number Needed to Treat (NNT) is therefore 200 per year to prevent one stroke. Thus the annual cost of this treatment associated with preventing one stroke, despite its significant reduction in stroke reduction (p=0.032) would be:

200 patients x £100 = 20,000.

---

32. A study of an established antihypertensive agent against placebo reports that the risk of death due to cardiac causes is lower on treatment. It gives 5-year mortality due to cardiac causes as 12% on placebo and 8% on treatment. The authors conclude that 'a 33% reduction in cardiac deaths is seen with treatment'.
The figure '33%' represents which of the following?

Available marks are shown in brackets
1) Absolute Risk Reduction [0]
2) Control Event Rate [0]
3) Experimental Event Rate [0]
4) Number Needed to Treat [0]
5) Relative Risk Reduction [0]

answer 5

An understanding of quantities discussed in 'Evidence-based medicine' is becoming increasingly important for the exam. If a drug reduces the incidence of heart attacks from 10% to 5% then ...
• the control event rate (CER) is 10%
• the experimental event rate (EER) is 5%
• the relative risk reduction (RRR) is 50%
• the absolute risk reduction (ARR) is 5%
• the number needed to treat (NNT) is 100% / 5% = 20

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33. A study of an established antihypertensive agent against placebo reports that the risk of death due to cardiac causes is lower on treatment. It gives 5-year mortality due to cardiac causes as 12% on placebo and 8% on treatment. The authors conclude that 'a 33% reduction in cardiac deaths is seen with treatment'.
The figure '33%' represents which of the following?

Available marks are shown in brackets
1) Absolute Risk Reduction [0]
2) Control Event Rate [0]
3) Experimental Event Rate [0]
4) Number Needed to Treat [0]
5) Relative Risk Reduction [0]

answer 5

Comment: An understanding of quantities discussed in 'Evidence-based medicine' is becoming increasingly important for the exam. If a drug reduces the incidence of heart attacks from 10% to 5% then ...
• the control event rate (CER) is 10%
• the experimental event rate (EER) is 5%
• the relative risk reduction (RRR) is 50%
• the absolute risk reduction (ARR) is 5%
• the number needed to treat (NNT) is 100% / 5% = 20

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34. In a study of 1000 subjects with adrenal incidental tumours, a new serological marker for adrenal carcinoma was assessed against formal histology. The following results were obtained:

Test positive Test negative Histology positive 40 10 Histology negative 50 900

To what does the specificity approximate?

1) 50% [0] 2) 60% [0] 3) 70% [0] 4) 80% [0] 5) 90% [0]

answer 5

Comments:

Sensitivity relates to the probability that the person with a disease will be correctly identified with the disease. Therefore, in this study, 50 subjects have adrenal carcinoma, of whom 40 are correctly identified with the disease giving a sensitivity of 80%. The specificity is the probability that a person without the disease will be correctly identified by the test. In this case, there are 950 subjects without adrenal carcinoma of whom 900 were identified by the test – giving a specificity of ~95%.

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35. A new test is developed for the diagnosis of HIV. Blood from 10,000 patients were analysed by the gold standard technique and by the new method. There were 100 positive results with the gold standard technique but there were 150 positive results using the new technique. Approximately which of the following values reflects the positive predicitve value of the new technique.

Available marks are shown in brackets

1) 33% [0] 2) 50% [0] 3) 66% [0] 4) 75% [0] 5) 90% [0]

answer 3

Comments: The positive predictive value is Number of True Positives/(No of true positives + False positives). In the new technique there were 100 true positives and 50 False Positives. Thus the positive predicative value is 66%

---

36. Which of the following statements is true regarding statistical interpretation of data?

Available marks are shown in brackets
1) The incidence equals the number of newly affected individuals divided by the number of people at risk for the disease for a given duration. [0]
2) The prevalence is readily distinguished from the incidence in relation to cancers. [0]
3) The mortality rate is a kind of cumulative prevalence rate. [0]
4) The cumulative incidence rate is usually given over a 10 year period. [0]
5) The prevalence rate is defined as the total number of cases divided by the total number in the population. [0]

answer 1

Comments: The incidence can be thought of as the number of new cases occurring in a given time. The cumulative incidence rate is usually reported over a year. Prevalence equals the total number of cases divided by the total number of at risk. In diseases for which the exact onset cannot be determined such as cancers, it may be difficult to distinguish between incidence and prevalence. Mortality rate is a special kind of cumulative incidence rate, with deaths in the numerator and population in the denominator. Case fatality rate, has deaths in the numerator and the number of people with a specific disease in the denominator.

---

37. A clinical investigation examined the effectiveness of a new test for diagnosing Pancreatic carcinoma. The sensitivity was reported as 70%. Which one of the following statements is correct?

Available marks are shown in brackets

1) 70% of people will be correctly classified as having or not having the disease [0]

2) 70% of people with an abnormal test result will have the disease [0]

3) 70% of people with a normal test result will not have the disease [0]

4) 70% of people with the disease will have an abnormal test result [0]

5) 70% of people with the disease will have a normal test result [0]

Answer 4

Comments: Sensitivity is the conditional probability that the test will be positive if the condition is present). Specificity is the conditional probability that the test will be negative if the condition is absent. Therefore, interpreting the data there is a 70% probability of the test being positive when tested in a group of patients with the disease

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38. A new publication describes a new test for cystic fibrosis. You want to know what proportion of patients with cystic fibrosis who would be correctly identified by this new test. Which one of the following values would identify this?

Available marks are shown in brackets

1) accuracy [0]

2) negative predictive value [0]

3) positive predictive value [0]

4) sensitivity [0]

5) specificity [0]

Answer 4 Comments:

The proportion of patients with the disease who would be identified by the new test is the sensitivity. This refers to the proportion with the disease who truly have cystic fibrosis and are identified as such by the test. Positive predictive value refers to the percent of people having a positive test who actually have the disease interpreted in conjunction to the prevalence of the disease (True positives/True positives + False positives)

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39. A randomized, double-blind, placebo controlled trial of a cholesterol lowering drug in the primary prevention of coronary heart disease is reported.
1000 subjects are treated with the active drug, and 1000 are given placebo. They are followed up over a five year period and 100 individuals in the placebo group and 80 in the treatment group suffer a myocardial infarction.
What is the annual percentage risk of myocardial infarction in the group treated with placebo?
1) 0.5% [0] 2) 2% [0] 3) 5% [0] 4) 8% [0] 5) 10% [0]

answer 2

Comments: Why this question is in the MRCP exam is anyone's guess! This is more of a mathematics exam. In the 5 years 100 patients in the placebo group develop an MI. Assuming this is spread evenly across the years this means that 20 patients (out of 1000) suffer an MI each year. The annual risk is therefore 20/1000 = 0.02 which, expressed as a percentage is 2.

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40. A randomized double-blind placebo controlled study of a cholesterol-lowering drug in the primary prevention of coronary heart disease was conducted over a five-year follow up period. The absolute risk of myocardial infarction in the group-receiving placebo during this time was 10 per cent.
The relative risk of those given the cholesterol lowering medication was 0.8.
What number of patients will need to be treated with active drug for five years to prevent one myocardial infarction?
1) 20 [0] 2) 40 [0] 3) 50 [0] 4) 80 [0] 5) 100 [0]

Answer 3

Comments:
The absolute risk of MI in the treatment group is 10% x 0.8 = 8% (as they have a relative risk of 0.8 as compared to the placebo group). NNT = 1 / absolute relative risk. ARR is the risk in treated group - risk in control group. Therefore the ARR is 10% - 8% and the NNT for that period is 1/0.02 = 50

==========

41. In a recently published clinical trial comparing rivaroxaban versus placebo in patients with recent acute coronary syndrome (ACS), the authors reported that the risk of myocardial infarction (MI) in the rivaroxaban group was 3.76% (384 MI's out of 10,225 patients) in the rivaroxaban-treated patients and 4.47% (229 MIs of 5125 patients) in the placebo-treated patients. What is the number of patients with recent ACS that would need to be treated (NNT) to reduce the risk of one MI?

A. 70 B. 85 C. 140 D. 195

Answer: C

ARR=0.0447-0.0376=0.0071
NNT= 1/0.0071=140

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42. In a meta-analysis of cohort studies examining the effects of several antihypertensive drugs, the odds ratio (OR) for treatment with low-dose diuretics compared with calcium channel blockers for cardiovascular disease events was 0.84 (CI, 0.75–0.95). Which statement is the most appropriate interpretation of these findings?

A. Treatment of hypertension with low-dose diuretics was 16% more effective in preventing cardiovascular disease events than treatment with calcium channel blockers
B. Treatment of hypertension with calcium channel blockers was 16% more effective in preventing cardiovascular disease events than treatment with low doses of diuretics.
C. The difference observed between treatment with calcium channel blockers and low doses of diuretics is not statistically significant
D. The odds of developing cardiovascular events when treating hypertension with low doses of diuretics are lower than when using calcium channel blockers.

The right answer is D

- Cl not contain 1 >>>>> So the test is statistically significant C.... is wrong
- If he use in the case RR instead of OR so 1. ... is right as we can calculate RRR 1-0.84=0.16= 16%
- If he use RR & Compare calcium channel blocker to diuretic So B..... is right
- In this case we can say Treatment HTP with low dose diuretics was from 5% to 25% more effective in preventing cvs event then use Ca channel blocker

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43. Which one of the following statements is the best interpretation for an OR of 4.0?

A. The odds of having the outcome among individuals who received treatment A are 10% higher than the odds among individuals who received treatment B.

B. The odds of having the outcome are 75% lower in individuals who received treatment A than those in individuals who received treatment B.

C. The odds of having the outcome among individuals who received treatment B are 10% lower than the odds among individuals who received treatment A.

D. The odds of having the outcome are 400% higher among individuals who received treatment A than those among individuals who received treatment B.

➢ Answer: D

- **Answer D** (the odds of having the outcome among individuals who received treatment A are 400% higher than in those in individuals who received treatment B) is correct because the OR is an estimate of the odds of the outcome in individuals in one treatment group compared with individuals who received the other treatment. This answer represents the correct interpretation of an OR of 4.0.
- **Answer A** (the odds of having the outcome among individuals who received treatment A are 10% higher than the odds in individuals who received treatment B) is incorrect because an OR of 1.1 is consistent with 10% higher odds of having the outcome among individuals who received treatment A than the odds of the outcome in individuals who received treatment B.
- **Answer B** (the odds of having the outcome are 75% lower among individuals who received treatment A than those among individuals who received treatment B) is incorrect because this answer is consistent with an OR of 0.25.
- **Answer C** (the odds of having the outcome among individuals who received treatment B are 10% lower than the odds among individuals who received treatment A) is incorrect because this is consistent with an OR of 1.1

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44.A new antipsychotic drug was compared with a previously available drug in a prospective, randomized, and blinded trial. This 12-mon trial measured the frequency of inpatient psychiatric admissions both treatment groups. At the end of the trial, 6% of the patients taking the new drug had an inpatient psychiatric admission compared with 11% of the patients taking the older drug (p=0.03). In presenting the results of this trial to members of the formulary committee with the health maintenance organization where you work, Which or of the following statements would provide the committee with the best information to use in deciding the formulary status of the new drug?

A.The new drug decreased psychiatric admissions by 45%.

B.The new drug decreased psychiatric admissions by 83%.

C.You would need to treat two patients with the new drug to avoid one admission.

D.You would need to treat 20 patients with the new drug to avoid one admission.

Answer: D

- This question addresses concerns about presenting data as either relative changes or absolute changes.
- Because relative changes give no indication of the baseline frequency of an outcome, they should not be used as the sole basis for clinical or drug policy decisions; therefore, **Answer A is incorrect**. This representation of differences in hospitalization rates is the relative change that occurred between the two groups. It is the result of dividing the observed difference in admissions (5%) by the baseline rate (11%).
- **Answer B** represents the miscalculation of the relative change where the difference in admissions was divided by the rate of admissions in the group receiving the new drug.
- **Answer C and Answer D** both come from attempts to calculate the number needed to treat from the absolute difference in events between the groups. The number needed to treat is the reciprocal of the absolute difference between groups.
- **Answer C** is a miscalculation of that value, resulting from a misplaced decimal when converting 5% to its decimal form (i.e., a conversion to 0.5 instead of 0.05).
- **Answer D** is the best answer and reports the correctly calculated number needed to treat of 20 patients to prevent one admission.

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45.A study reports an odds ratio of 1.18 for ventricular arrhythmia associated with the use of a recently marked diuretic when compared to hydrochlorothiazide. The 95% confidence interval reported for this odds ratio is 1.04 to 1.33. Which one of the following is the correct interpretation of these results?

A.the risk of ventricular arrhythmia may be decreased between 4% and 33% with the use of this new diuretic when compared to hydrochlorothiazide

B.the risk of ventricular arrhythmia may be 4 to 33 times less with the use of this new diuretic when compared to hydrochlorothiazide

C.the risk of ventricular arrhythmia may be elevated between 4% and 33% with the use of this new diuretic when compared to hydrochlorothiazide

D.the risk of ventricular arrhythmia may be 4 to 33 times greater with the use of this new diuretic when compared to hydrochlorothiazide

- **Answer:**
  - CODDs ratios are compared to baseline risks of one for their interpretation. Numbers greater than one indicate an increased risk while numbers less than one indicate a decreased risk.
  - In this question an odds ratio (OR) of 1.18 indicates a potentially increased risk. As such, answers **a and b are incorrect.**
  - **Answer d** (4 to 33 times greater risk) is consistent with a confidence interval for the OR of 4.0 to 33.0.
  - A confidence interval of 1.04 to 1.33 means that the risk of ventricular arrhythmia may be increased anywhere from 4% to 33% when compared to the baseline risk of using hydrochlorothiazide **(answer c)**.

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46. A study reports an increased incidence of falls associated with the use of a certain type of antidepressant. The study selected groups of patients based upon whether or not they had received medical care for a fall in the previous 3 years. Patients in both groups (i.e., those with a fall or those without a fall) were matched based on their age, preexisting psychiatric and medical conditions, other medications, and sex. Which one of the following represents the type of trial design used in the above investigation?

A. prospective cohort
B. retrospective cohort
C. case-control
D. randomized, controlled trial

- **Answer: C.**
  - In this trial, participants are divided into two groups based on whether or not they experienced a particular clinical event (i.e., a fall). Both groups, those experiencing a fall during the study period and those not experiencing a fall during the study period, are assessed for their use of a particular type of antidepressant.
  - This description is consistent with a case-control design (answer c). In a cohort trial, patients are grouped based on their exposure (e.g., to a certain type of drug) and then followed to see if they experience a particular clinical event (e.g., a fall).
  - In a prospective cohort trial (answer a) the exposure happens in the past, but the event may occur in the future as patients are followed prospectively through time.
  - In a retrospective cohort design (answer b), both the exposure and outcome have already occurred.
  - A randomized, controlled trial (answer d) assigns people to groups randomly and no part of the study is based upon retrospective observations.

==========

47. A randomized, controlled, double-blind trial is designed to test the difference in clinical response rate between erythromycin 500 mg TID and amoxicillin 500 mg TID, when used in the empirical treatment of acute upper respiratory infections in children. Based on the information provided, which one of the following would be suspected as a likely weakness of this study, even before reviewing the results?

A. the use of surrogate markers
B. the ability to blind the study
C. the large number of secondary outcomes
D. the use of appropriate statistical tests

- Answer: B.
  - While any of the answers can be a concern for a randomized trial, in this case the ability to blind the study (answer b) stands out as a concern.
  - Here investigators are using two drugs that have very different side-effect profiles. Because erythromycin has a very high incidence of nausea and gastrointestinal distress associated with its use, it is likely to be difficult to blind effectively.
  - There is no mention of surrogate markers (answer a) or secondary outcomes (answer c) for this study. We have no reason to believe before reviewing the study that the use of appropriate statistical (answer d) tests would present a particular challenge.

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48. A trial compared the effect of an adherence reminder postcard on the percentage of patients who had their prescriptions refilled on time. Two pharmacies within 2 miles of each other and from a single chain where recruited to participate. Each pharmacy measured refills for 1000 patients. The results after one month are listed in the table below. Pharmacy Refilled on time late refill Reminder card 876 124No reminder card 629 371The difference between groups is listed as statistically significant with a p-value of less than 0.0001. How many of these postcards will need to be sent to result in one additional on time refill?

A. 4 B. 8 C. 40 D. 247

- **Answer: A.**
  - This question asks you to calculate a "number needed to treat" (NNT). In this case, however, it is calculated for a dichotomous, non-clinical outcome (i.e., on time versus late refill).
  - The calculation is the same as any NNT calculation and takes the form of the reciprocal of the absolute difference in outcomes. Pharmacy Refilled on time Late refill Reminder card 876 124No reminder card 629 371For this data the calculation would be set up as NNT = 1/87.6% -62.9% = 1/0.876-0.629= 1/0.247 = 4.04. Therefore the correct answer is 4 (answer a).

==========

49. Which of the following is correct concerning an Intention To Treat analysis?

1) It is a variation of a meta-analysis analyzing specifically studies employing double blind placebo controlled trials. [0]

2) It is a study where all included patients are treated with the active drug. [0]

3) It is a study where all non-compliant patients are removed from analysis. [0]

4) It is a study that analyses all patients randomized to the study. [0]

5) It is a study comparing the effects of treatment with placebo or active treatment and also a similar group of non-study participants. [0]

- Answer 4
- Comments:
  - When one considers a randomized study, although the principles of double blind placebo controlled may apply, the actual preferential fall out of patients, for instance treated with placebo as they do not perceive a benefit, may itself introduce bias.
  - Thus, Intention to treat studies would argue that one should commit all patients that originally participate in the study to analysis.
  - The advantages of this approach are that it maintains treatment groups that are similar apart from random variation.
  - This is the reason for randomization, and the feature may be lost if analysis is not performed on the groups produced by the randomization process. Secondly, it permits for non-compliance and deviations from policy by clinicians.

==========

50. In a chronic disease which has no known effective treatment, a new treatment is known to be effective in animal models and shows promise in short-term studies in patients. There are some theoretical concerns about toxicity involving liver and bone marrow although no cases have been observed in studies so far.
What is the most appropriate next step in the drug's development?
1) case control study [0]
2) No further studies should be done and drug development should be stopped [0]
3) open study [0]
4) randomised double blind placebo controlled study [100]
5) randomised single blind placebo controlled study [0]

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51. The absolute risk reduction in mortality when utilizing internal cardioverter-defibrillator devices in New York Heart Association Class II or III heart failure patients with a left ventricular ejection fraction < 35% compared to placebo was 7.2% after 5 years of follow up (28.9% versus 36.1%, respectively). Which one of the following is the number of patients needed to treat to prevent one future death?

A. 3 B. 4 C. 14 D. 125

- Answer: C.
- Comment: The number needed to treat is calculated by 1/ARR (ARR=absolute risk reduction). Since the absolute risk reduction in death was 7.2%, (1/0.072) = 14 patients would need an internal cardioverter defibrillator to prevent one death from arrhythmia.

==========

52. In a study of 26000 females, 1300 subjects were found to have either overt or subclinical hypothyroidism. Within this group, the risk of demonstrating either overt or subclinical hypothyroidism was therefore 5%. What is the best descriptive term of this 5% risk?

A.Absolute risk B.Incidence C.Prevalence
D.Relative risk E.Specificity

- Answer : C
- Comment: This is the risk of either subclinical or overt hypothyroidism in a female population at any specific time which is the prevalence. This is defined as the rate of a disorder in a specified population at a specified time. Incidence refers to the number of new cases of a disorder developing over a specific time

53. A clinical trial assessing a new lipid lowering therapy for stroke allocates 1000 patients to active treatment and another 1000 patients to placebo. Results demonstrate that number needed to treat (NNT) is 20 for the prevention of the primary end-point. Which of the following best describes the results?

A. 20 patients in the treatment group were protected from stroke.
B. 20 extra patients in the placebo group had a stroke
C. For 1000 patients treated with active therapy, there would be 20 fewer strokes
D. For 1000 patients treated with active therapy, there would be 50 fewer strokes.
E. For every 1000 patients treated with active therapy there would be 100 fewer strokes

- Answer: D
- Comment: This prevention study for stroke reveals that 20 patients need to be treated to prevent one event. Thus if you treat a 1000 patients then you will expect to have 50 fewer strokes.

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54. A publication reports the outcome of a new statin therapy in a placebo controlled primary prevention of ischemic heart disease in a diabetic population. 1000 patients were randomized receive the new therapy and 1000 allocated to placebo. The study was completed over a five year period. In the placebo group there were 150 myocardial infarcts and in the group treated with the new statin there were 100 infarcts. What is the relative risk reduction of MI afforded by statin therapy?

A. 15% B. 25% C. 33% D. 40% E. 50%

- Answer : C
- Comment:
  - There are 50 fewer MIs in the treated group then the placebo treated group, hence 50/150=33%. The relative risk reduction provides information regarding the efficacy of a therapy and what reduction in risk may be expected when treating subjects rather then just having data relating to the significance of the data.
  - RR =0.1/0.15 = 0.66, RRR= 1-0.66=0.33 "33%"

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55. A randomized, double-blind, placebo-controlled study was conducted to determine whether metoprolol decreased the composite outcome of death, ventricular tachycardia, myocardial infarction, hospitalization, angina, and cardiovascular revascularization. At the end of 1 year, the metoprolol-treated group experienced fewer composite outcomes than the placebo group (11% vs. 25%, respectively). The relative risk of those who were in the metoprolol group was 0.44 (95% confidence interval, 0.26–0.75). According to these data, which one of the following best represents the number of patients needed to treat with metoprolol to prevent one of the listed outcomes?

A. One. B. Three. C. Four. D. Eight.

- Answer D: Eight.
- Comment: The number needed to treat is calculated by taking the reciprocal of the absolute difference in treatment arms for a given outcome. In this case, 25% minus 11% gives 14%. The reciprocal of 14% (1/0.14) = 7.14 or rounded up eight patients treated

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56. As a member of a clinical trials group at a large pharmaceutical company, you are asked to design a study to ascertain whether a link exists between new-onset bronchospasm and a newly marketed drug for the treatment of ALS (acute lateral sclerosis). The U.S. Food and Drug Administration (FDA) has expressed concern about data that suggest a trend toward increased risk of bronchospasm, observed in early clinical trials; therefore, the FDA has asked for some phase IV data after marketing. Which one of the following should be suggested as the most appropriate study design?

A. A case series.
B. A randomized, controlled trial.
C. A prospective cohort study.
D. A retrospective cohort study.

- Answer D:
- Comment:

- Bronchospasm is a common disorder; however, ALS is uncommon, and thus, exposure to this agent would be uncommon, too. This study lends itself to a cohort trial.
- A prospective cohort would potentially take longer to conduct; thus, a retrospective cohort would be chosen

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57. A study is designed to investigate the number of adverse drug events in a group of individuals during a 1-year period. In the results, the authors report that five events occurred per 10,000 person-years. Which one of the following measures does this estimate represent?

A. Relative risk.
B. Incidence rate.
C. Odds ratio.
D. Prevalence.

- Answer B: Incidence rate.
- Incidence rate is a measure of the instantaneous rate of developing a disease. It is estimated by divining the number of individuals who develop a disease by the total amount of time that these individuals were at risk for developing a disease. The prevalence is a measure of the number of individuals who have a condition/disease at any given time. Both relative risk and odds ratio estimate the magnitude of association between exposure and disease.

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58. You are one of the pharmacists on the Pharmacy and Therapeutics Committee. A formulary drug is being scrutinized because of rare reports of serious drug-induced rhabdomyolysis. The FDA is reevaluating the safety of the drug, but that reevaluation is likely to take a considerable amount of time. The committee is considering whether to take a drug off the formulary. Which one of the following study designs would you consider best suited for this problem?

A. Randomized, controlled crossover clinical trial.
B. Case-control study.
C. Prospective cohort study.
D. Randomized, controlled parallel-group clinical trial

- Answer B: Case-control study.
- A case-control is the most appropriate study design in this situation since this study would be investigating a relatively common exposure (drug is on the market and being routinely used clinically) and relatively rare /uncommon outcome. Neither A nor D would be ethically possible, since we know there is a published rare, but serious toxicity. Additionally, A, D and C are incorrect in that these designs would also take a considerable amount of time to conduct

59. The results of a randomized controlled trial between two drug treatments for depression describe no difference in responses between the two groups (p=0.30). The study authors report that they subsequently carried out an analysis of subgroups based on the following: subjects with past episodes of depressive episodes, subjects with a family history of depression, and subjects who were women. They found a significant difference in response between the two treatments ($p<0.05$) for men versus women. Reviewing this study with a group of pharmacy students, which one of the following best describes what the students should know?

- A. The finding of a difference between men and women in this study should be tested in a prospective study.
- B. Post hoc subgroup analyses are generally useful for showing differences between subgroups of patients.
- C. There is no need to make statistical adjustments when comparing the results of each of these subgroups.
- D. It is expected that men and women will respond differently to depression pharmacotherapy

- Answer A:
- Comments: Subgroup analyses are vulnerable to many problems in interpretation. In general, those not specified at the start of the study are likely to suffer from issues of power and the absence of correction to the statistical analysis to account for multiple subgroup comparisons. Findings from post hoc analyses are best viewed as presenting questions for further study like other observational studies, not as answers to questions themselves.

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60. Several cases in the literature have described retinal detachment associated with fluoroquinolone antibiotics. A study is being designed by a U.S. drug manufacturer to investigate this phenomenon. Which one of the following study designs represents the best approach for studying this drug-associated adverse event further?

A. Cross-sectional study.
B. Prospective cohort study.
C. Retrospective case-control study.
D. Randomized controlled trial.

- **Answer C:** Retrospective case-control study.
- **Comments:**

- Each of these study designs may add important information, but **the case-control design** offers the advantages of being relatively inexpensive and of being conducted reasonably quickly. More importantly, **the case-control study** is most appropriate in conditions that are rare or that occur infrequently. This adverse event associated with fluoroquinolones is uncommon.
- **A cross-sectional study** would only provide a snapshot in time and might not detect the outcome of interest. **A randomized clinical trial** is not ethnically reasonable because of the negative outcome that would need to be investigated, nor would it be practical.
- **A prospective cohort study** would be more expensive and time-consuming to complete.

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61. The FDA has requested that a pharmaceutical manufacturer conduct a phase IV study of a recently approved drug. The FDA is interested in determining whether this drug reverses left ventricular diastolic dysfunction. Which one of the following study designs represents the best approach for studying the temporal relationship between the drug and left ventricular diastolic dysfunction?

- A. Randomized, controlled, crossover trial.
- B. Case-control study.
- C. Prospective cohort study.
- D. Cross-sectional study

- **Answer C:** Prospective cohort study.
- **Comment:** To study the temporal effects, only **a randomized controlled trial** or **prospective cohort study** would be appropriate. Although a randomized controlled trial might be appropriate, a crossover trial would not be appropriate in this situation because of the changing disease process. **A cross-sectional study** would only provide a snapshot in time and might not detect the outcome of interest. **A prospective cohort** study is most appropriate.

62. Which one of the following will be most affected by the type of bias likely to occur in this study?

A. External validity.

B. Internal validity. (B)

C. Assessment of exposure.

D. Number of patients needed for the study.

==========

63. An oncologist has gained the impression that many women diagnosed as having breast cancer also have high levels of work-related stress. What type of design would be the most practical to test this possible association?

A. Group comparative, randomized controlled trial

B. Cross-over, randomized cross-over trial

C. Prospective cohort study

D. Retrospective case-control study (D)

E. Prospective observational study

==========

64. A letter published in a journal suggests an established antidepressant may cause photosensitivity. The manufacturer wishes to determine as rapidly as possible whether this a true association. Which one of following techniques is most appropriate?

a)Case-control study

b)Dose-ranging study

c)Double-blind, randomized, placebo-controlled study

d)Meta-analysis

e)Sequential trial

==========

65.A randomized controlled trial comparing a new drug for seasonal rhinitis to current best treatment uses an equivalence design, concluding that the two treatments are equivalent. Which of the following statements best describes the results of the trial?

a)The 95% confidence interval for the treatment effect fell entirely within pre-specified limits (A)

b)The design of the study was inappropriate as neither treatment was compared to placebo

c)The outcomes in the two arms of the trial were identical

d)The results of the study were inconclusive, indicating that a larger study needs to be performed

e)There was no statistically significant difference between the two treatments

==========

66. In a randomized controlled trial of a new treatment for preventing recurrence of stroke, 1000 patients are randomized to the new treatment and 1000 to standard therapy. A total of 66 patients receiving the new treatment suffered recurrent stroke, compared to 110 in the control arm. What was the relative risk reduction?

A.4.4%

B.6.6%

C.11%

D.40%

E.60%

RRR=(C/C+D)-(A/A+B)/(C/C+D)=(110/1000)-(66/1000)/(110/1000)=0.4*100=40 %

Risk Factor	Disease		
	+ VE	- VE	
+ VE	66		1000
- VE	110		1000

---

67. Ultrasound scanning at 20 weeks was found to correctly detect 35 of the 50 babies ultimately diagnosed as having a congenital heart defect. However, five of the 500 babies born with no congenital defect were also recorded as problematic when screened. Which of the following is a correct statement of the properties of ultrasound scanning as a screening test for congenital heart defects?

A. Positive predictive value = 70%; negative predictive value = 99%

B. Positive predictive value = 70%; negative predictive value = 1%

C. Sensitivity = 70%; specificity = 99%

D. Sensitivity = 70%; specificity = 1%

E. No test properties can be estimated as these are all affected by the prevalence of congenital heart defects in the study population - this figure is not given

- Answer

- sensitivity=a/a+c=35/50=70%>>>>>>>> specificty=d/c+d=495/500=99% so answer C

New test	Reference test		
	Disease +ve	Disease – ve	
Disease +ve	A 35	B 5	
Disease – ve	C 15	D 495	

==========

68. You are drawing up a trial of a new screening test. If the threshold of the screening test is increased, which of the following would increase?

A. Sensitivity B. Specificity C. Prevalence

D. Negative predictive value E. Positive predictive value

ANSWER C

==========

69. If screening for breast cancer by mammography has a sensitivity of 75% and a specificity of 95% in a certain population, what is the positive predictive value?

A.1/16 B.5/24 C.19/24

D.15/16

E.There is not enough information to calculate the positive predictive value (answer E)

==========

70. A 73-year-old man is admitted to the hospital after suffering a left carotid territory stroke. His blood pressure is 155/90 mmHg and he is in sinus rhythm with a pulse of 65 bpm. On carotid duplex it appears there is a stenosis which is amenable to surgical therapy. He asks you about the risks of surgery versus intensive medical therapy. On reviewing the trials you note that the incidence of stroke in the surgical intervention group was 8%, versus 18% in those who had medical intervention only. How would you calculate the number needed to treat over 2 years with surgery to prevent 1 stroke?

A.100/(18-8)

B.18/8

C.100/(18/8)

D.18-8

E.100-(18/8)

- ARR=18-8/100>>>>> NNT=1/ARR=100/18-8 SO (ANSWER A)

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71. A study is planned into the effects on risk of myocardial infarction of a new lipid modifying agent, and the steering committee states that they plan to include number needed to treat (NNT) as part of the primary manuscript. How is the number needed to treat over the duration of the study calculated?

A. Ratio of absolute to relative risk reduction

B. Ratio of relative to absolute risk reduction

C. Reciprocal of relative risk reduction

D. Reciprocal of absolute risk reduction (D)

E. Number of months of study divided by the absolute risk reduction

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72. In a trial of a new drug compared to standard therapy, the risk of complications in the control arm is 2.4% and the risk of complications in the treatment arm is 1.8%. What is the absolute risk reduction associated with the new treatment?

A.0.6% B.1.8 C.2.4% D.25% E.33%

ARR = 2.4-1.8 = 0.6%

==========

73. Vignette:In a prospective, randomized, double-blind trial, researchers compared the effects of two different methylprednisolone doses on neurologic and safety outcomes in patients with acute spinal cord injury. One treatment arm received a bolus of 1000 mg followed by 250 mg every 6 hours for 10 days (high dose; n=151). The other treatment arm received an intravenous bolus of 100 mg followed by 25 mg every 6 hours for 10 days (low dose; n=153). During this study, wound infections developed in 9.3% of patients in the high-dose group compared with 2.6% of patients in the low-dose group (95% confidence interval, 1.2–10.59).Which statement regarding the relative risk between the two treatment groups for developing wound infections is correct?

A- Patients in the high-dose group were 3.5 times more likely to develop a wound infection ($p<0.05$).

B- There is no difference in the risk of developing a wound infection between groups.

C-Information is insufficient to determine relative risk, but the difference is statistically significant.

D- Information is insufficient to determine relative risk or whether the difference is statistically significant.

- answer A>>>>>>>>>>>>>>>>>>>>..
- The prevalence of wound infections was 9.3% versus 2.6% in the high-dose versus low-dose group, respectively. Dividing 9.3 by 2.6 will determine the relative risk (9.3/2.6 = 3.5); therefore, options C and D are incorrect. Because the confidence interval does not cross 1, it should be determined that the difference is, in fact, statistically significant.
- A p-value of <0.05 corresponds to the 95% confidence interval provided in case. Therefore, option A is correct. Option B is incorrect because there is a clinically and statistically significant difference in risk for would infections between groups
- (i.e., high-dose group was 3.5 times more likely to develop a wound infection, p<0.05).

==========

74. Vignette: A randomized, double-blind trial compared eplerenone with placebo in patients with New York Heart Association class II heart failure and reduced ejection fraction. The incidence of death from any cause was 171 of 1364 (12.5%) in the eplerenone group and 213 of 1373 (15.5%) in the placebo group, a statistically significant difference (adjusted p=0.008). Which represents the number of patients who would need to be treated to prevent one death with eplerenone use?

A.14 B.34 C.42 D.102

- **Answer B.**
- Comment:

- The NNT is determined by first finding the incidence of the outcome (death in this case) in each treatment group, then simply finding the difference in the incidences between the groups and then simply dividing 1 by this difference (in decimal format).
- In this item, the incidence of death in the eplerenone group is determined by dividing the number of deaths that occurred in this treatment group (N=171) by the total eplerenone treatment group who were at risk of incurring death (N=1364, therefore 171/1364=0.125 or 12.5%). This process is repeated for the incidence calculation for the placebo group (213/1373=0.155 or 15.5%).
- The next step would be to determine the difference in these incidence values, called the Absolute Risk Reduction (ARR). This difference, or ARR, is calculated by simply subtracting the incidences between groups (i.e., 0.125-0.155=-0.03).
- The NNT is then determined by simply dividing 1 by the ARR (i.e., 1/-0.03=-33.3). NNT's are always reported in whole patients. Therefore, the correct answer for this item is 34 patients. All other answer options are incorrect.
- The interpretation of the NNT is as follows: Based on the differences in the incidence of death between the treatment groups, 34 patients would need to be treated with eplerenone to prevent 1 death. The other answers are incorrect.

Or simply

- ARR, is calculated by simply subtracting the incidences between groups (i.e., 0.125-0.155=-0.03). The NNT is then determined by simply dividing 1 by the ARR (i.e., 1/-0.03=-33.3)

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75. Vignette:You have anecdotally observed several members of the nursing staff improperly preparing and administering several intravenous medications possibly leading to adverse drug events. Some examples of medication errors you have observed are: daptomycin accidently reconstituted with D5W instead of normal saline prior to dilution and compatibility issues when administering midazolam with TPN. Your goal is to gain further insight into the frequency of administration medication errors in the ICU at your hospital. Which of the following detection methods would be most appropriate?

A. Patient and family interview

B. Direct observation

C. Solicited voluntary reporting

D. Retrospective chart review.

- Answer B.
- Comment:

- Direct observation would be the ideal detection method (Answer B correct). Although patient and family interviews are useful in detecting adverse drug events in an ICU setting, this approach may not be the most suitable for detecting medication administration errors that occurred without an actual adverse event taking place **(Answer A incorrect).**
- Relying on voluntary reporting from the nursing staff is not the most reliable method because adverse event documentation is traditionally quite low, given that it is a time-consuming process together with the lack of initiation to complete the forms **(Answer C incorrect).**
- Retrospective chart review also has very low rates of documentation pertaining to adverse drug events as well as medication errors with no clinical consequences (**Answer D incorrect).**
- The nature of administration errors would be best detected by directly observing for these error types.
- Although the Hawthorne effect (i.e., changed behavior when being observed) is thought to occur, several reports have found that normal behavior is resumed a couple of hours after the observation period.

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76. The following table illustrates the findings of a hypothetical retrospective, cohort study in 100 subjects living in small villages in Ethiopia. Specifically, the study evaluated the frequency of disease following exposure to contaminated pond water. Based on this table, which of the following statements is most accurate in describing the risk ratio (RR) comparing disease between those subjects exposed and not exposed?

	DISEASED	NOT DISEASED	TOTAL
EXPOSED	42	2	44
NOT EXPOSED	21	35	56
TOTAL	63	37	100

A- Compared to those subjects who were not exposed, subjects exposed to the contaminated pond water were 2.55 times more likely to develop disease.

B- Compared to those subjects who were not exposed, those exposed to the contaminated pond water were 54% more likely to develop disease.

C- Compared to those exposed to the contaminated pond water, subjects who were not exposed were 62.5% less likely to develop disease.

D- Compared to those exposed to the contaminated pond water, subjects who were not exposed were 2.55 times more likely to develop disease.

- Answer :
  risk in exposed gp= 42/44=0.95
  risk in non exposed gp = 21/56=0.375
  RR = 0.95/0.375= 2.56

- Answer A,
- Comment:

- Since the risk ratio (RR) is a ratio of proportion, the calculation of the risk ratio (RR) is accomplished by first determining the risk of disease in the exposed group and the unexposed group, individually.
- This can be obtained by dividing the number of subjects who developed disease (in each of the 2 groups; exposed and unexposed) by the total study population (column totals; for those who were exposed and who were unexposed, respectively).
- Therefore, the risk of disease in the exposed would be (42/44=0.955) and the risk of disease in the unexposed would be (21/56=0.375). Then, ultimately, the RR would be (0.955/0.375=2.55).
- The secondary aspect of this correct answer is the ability to know which group is the reference group and which group is being compared to the reference group.

- In all situations, the reference group is the unexposed group and the comparison group is the exposed group.
- Therefore, the RR is the ratio of the exposed group (comparison group) to that of the unexposed group (reference group).
- Due to this fact, the summary statement of the RR is the RR of the exposed group compared to the unexposed group.
- This ordering of the statement is what makes choice "D" incorrect as it is stated backwards (wrong comparison group and wrong reference group; comparing the wrong group order).
- **"B" is incorrect**, yet plausible, due to the fact that even though the comparisons of groups were in the correct order (exposed group compared to the unexposed group), the calculation of the RR is incorrect.
- **"C" is incorrect**, yet plausible, due to the fact that the RR is incorrectly calculated; even though the comparison of groups is correct (exposed group compared to unexposed group).
- "**D" is incorrect**, yet plausible, because although the RR is calculated correctly, the phrasing of the interpretation of this RR is backwards (comparing the wrong group order).

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77. Vignette: A new therapy has been developed for the prevention of ventilator-associated pneumonia (VAP). In patients receiving standard therapy, the incidence of VAP is 20%. In patients receiving the new therapy, VAP incidence is 8%.

What is the number needed to treat of this new therapy to reduce VAP incidence?

A.6 B.8 C.40 D.60

- The correct choice is Answer B. The relative risk reduction is 60%, and the absolute risk reduction is 12%. The number needed to treat is 1/.12 = 8.3.

==========

78. Vignette: Results of an ICU study found patients receiving intensive insulin (glucose goal 81–108 mg/dL) are at significantly higher risk of hypoglycemia compared to patients receiving conventional (non-intensive) glucose control (goal glucose of 180 mg/dL). The trial randomized 6030 patients and reported that severe hypoglycemia (40 mg/dL or less) occurred in 206 of 3016 patients (6.8%) in the intensive-control group and in 15 of 3014 (0.5%) in the conventional-control group ($p<0.001$). What is the number needed to harm (NNH) associated with use of this intensive insulin approach?

A.3 B.6 C.16 D.36

- Answer C
- Comment: The NNH is a measure used to determine how many patients would be exposed to a certain risk factor or adverse effect with one therapy compared with a control group. Calculating this number is similar to calculating the number needed to treat (NNT).
  NNH = 1/(the proportion of patients with hypoglycemia with intensive insulin minus the proportion of patients with hypoglycemia with conventional therapy)
  The NNH is therefore 1/((206/3016) – (15/3014)).

==========

79. You would like to conduct a study on occurrence of pelvic inflammatory disease (PID) following insertion of two different intrauterine devices (IUD). The published incidence of PID following IUD insertion is 0.4% and you would like to investigate whether this varies based on the type of IUD inserted. Which of the following study designs would be most appropriate to accomplish your study objective?

A.Retrospective case-control study B. Retrospective cohort study

C. Prospective cohort study D. Prospective randomized controlled study

- answer A >>>>>>
- Comment: As the incidence of PID following IUD insertion is very low, a case control study would likely be the best study design. A case control study would also allow you to control for variables that may also increase risk of PID development. Since the incidence of PID development is so rare, a cohort study would not be appropriate. A large number of patients would need to be enrolled to complete a randomized controlled study on this subject.

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80. Vignette: In a trial investigating methylprednisolone infusions in early severe acute respiratory distress syndrome (ARDS), 91 patients with severe ARDS were randomized to receive a methylprednisolone infusion of 1 mg/kg/day versus placebo within 72 hours of diagnosis. For the end point of intensive care unit (ICU) mortality, the rate was significantly decreased in those who received methylprednisolone versus those who received placebo (20.6% vs. 42.9%, p=0.03). Which best describes the number needed to treat to avoid one ICU-related death?

A 1.9 B 4.5 C 22.3 D 52.0

- Answer B.
- Comment:

- To calculate the number needed to treat (NNT), the absolute risk reduction (ARR) must first be calculated.
- The ARR is the difference between the control event rate and the experiential event rate, or 22.3 (Answer C is incorrect).
- The NNT is the inverse of the ARR, or 1/ARR (Answer B is correct).
- From this information, the relative risk reduction (RRR) can also be assessed as the ARR divided by the control event rate (Answer D is incorrect).
- The 1/RRR is not routinely calculated (Answer A is incorrect).

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81. The Women's Health Initiative trial reported a 5-year incidence of one new fracture of 8.6% (733 of 8506) in the estrogen plus medroxyprogesterone group and 11.1% (896 of 8102) in the placebo group. Which best represents the number of patients needed to treat with estrogen plus medroxyprogesterone to prevent one additional fracture?

A 2 B 4 C 25 D 40

Answer D

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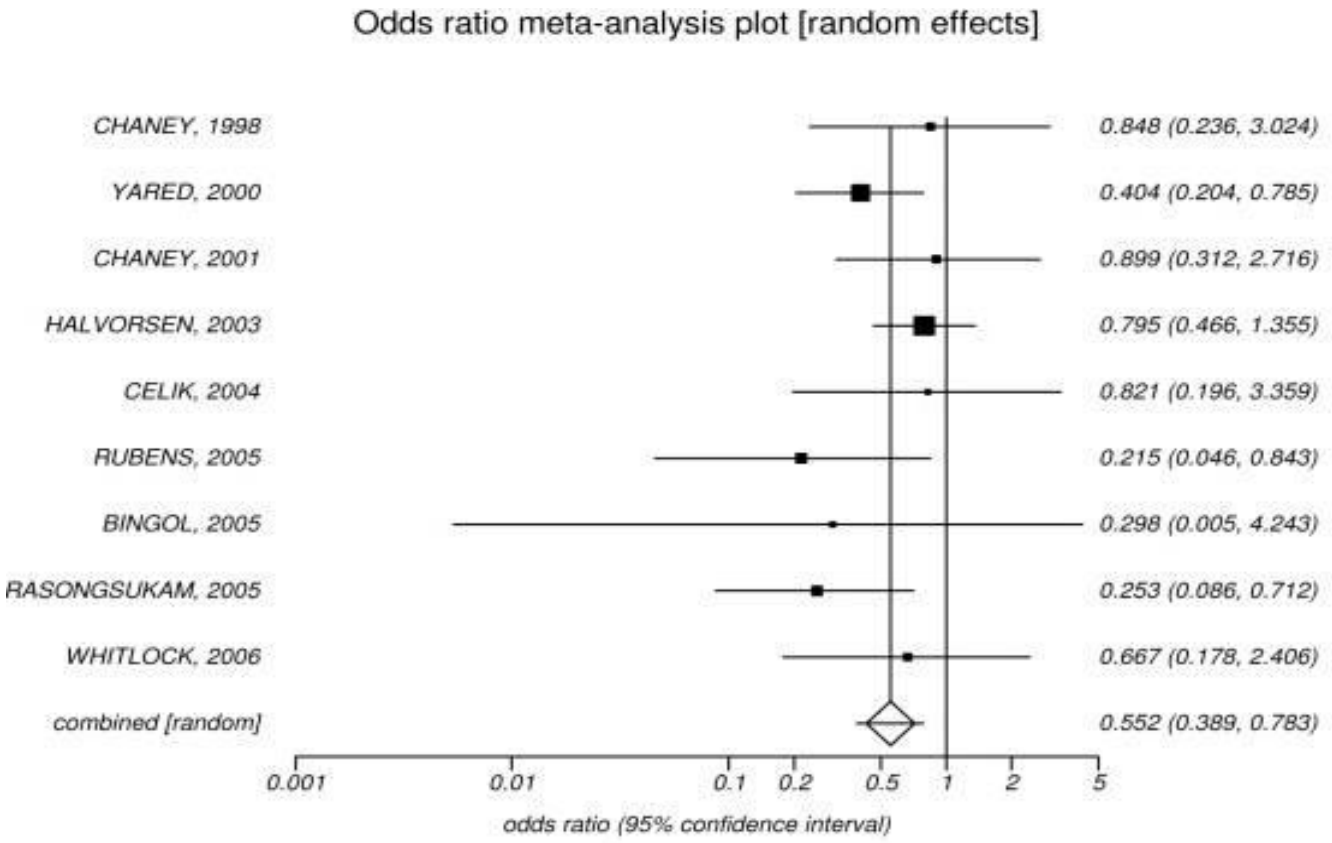
82. The figure below shows the results of a meta-analysis evaluating the impact of corticosteroids on the incidence of atrial fibrillation after cardiothoracic surgery. Which of the following is the best interpretation of these results?

A Corticosteroids increase atrial fibrillation odds by 55%.

B Corticosteroids reduce atrial fibrillation odds by 2-fold.

C Corticosteroids reduce atrial fibrillation odds by 45%.

D Corticosteroids have no significant effect on atrial fibrillation risk.



Answer C : This meta-analysis showed that perioperative use of corticosteroids reduced the odds of developing postoperative atrial fibrillation by about 45%. When evaluating ratio data (e.g., odds ratio, risk ratio), the line of unity is 1. Points below or above this line show reduced and increased odds, respectively. If the confidence interval horizontal line crosses 1, the effect is not statistically significant.

(Notes: increase box mean inc. sample size>>>>>>decrease bar mean dec. CI)

(if big box w small bar mean dec. range of CI<<<<<< if smal box w long bar mean inc. range of CI)

83. A study was designed to assess the association between glucocorticoid use and the development of acute pancreatitis. A total of 6,161 individuals with acute pancreatitis and 61,637 individuals without pancreatitis were enrolled and then the investigators looked retrospectively for differences in glucocorticoid use between the study groups.
Which option best describes this study design?

A Case series B Case-control

C Cohort D Cross-sectional

- Answer B.
- This is an example of a case-control study. Case-control studies are most appropriate when investigators want to study differences in exposure (and the presence of the outcome is known).

- In this item, investigators know if the patient has pancreatitis or not, and wish to evaluate the differences in glucocorticoid use (exposure). This is different from cohort studies which study differences in the outcome (and the presence of the exposure is known).
- A case series is when more than one patient with a similar experience is reported in a descriptive review.
- A cohort study would classify a patient population by whether patients received a corticosteroid and then determine whether they developed acute pancreatitis.
- A cross-sectional study is an evaluation of the prevalence or characteristics of a group of individuals at a particular time.

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84. In a recently published clinical trial comparing rivaroxaban versus placebo in patients with recent acute coronary syndrome (ACS), the authors reported that the risk of myocardial infarction (MI) in the rivaroxaban group was 3.76% (384 MI's out of 10,225 patients) in the rivaroxaban-treated patients and 4.47% (229 MI's out of 5,125 patients) in the placebo-treated patients. What is the number of patients with recent ACS that would need to be treated (NNT) to reduce the risk of one MI?

A 70 B 85 C 140 D 195

- Answer C
- The number needed to be treated (NNT) to reduce a single event is determined by subtracting the event rates in the two treatment groups (in decimal format), resulting in a value defined as the absolute risk reduction (ARR), and dividing 1 by this ARR value.
- Therefore, since the MI rate in the rivaroxaban-treated group was 3.76% (0.0376) and the MI rate in the placebo-treated group was 4.47% (0.0447), the clinician would simply subtract these two values (in decimal format; 0.0376-0.0447) to determine the absolute risk reduction (ARR) and then divide 1 by the ARR (1/ARR) to determine the NNT [(1/(0.0376-0.0447)].
- Since the denominator results in a negative value, this shows that the active treatment group (rivaroxaban) is beneficial (reduces risk of MI), yet you would have to treat 140 patients with this drug to prevent a single MI event.
- "A" is incorrect, yet plausible, since it is relatively similar in value yet was calculated by arbitrarily subtracting the percentage values of the respective group event rates and multiplying it arbitrarily by 100 [(4.47-3.76)x100=71; selected 70 to reduce test-wise direction towards the correct answer].
- "B" is incorrect, yet plausible, since it is relatively similar in value yet was calculated by arbitrarily dividing the percentage values of the respective group event rates and multiplying it arbitrarily by 100 [(4.47/3.76)x100=84; selected 85 to reduce test-wise direction towards the correct answer].
- "D" is incorrect, yet plausible, since it is relatively similar in value yet was obtained arbitrarily without a formal, incorrect calculation and to reduce test-wise direction towards the correct answer.

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85. Researchers conduct a study to determine the impact of potential risk factors on the occurrence of breast cancer. Of the techniques available to researchers useful for controlling for confounding variables, which of the following methods could ultimately reduce the external validity of their study?

A Matching
B Multivariate analysis
C Restriction
D Stratification

- Correct Answer: "C".
- There are 3-4 key ways for researchers to control for, or reduce the impact of, confounding variables. Of those, only restricting the study population to those individuals who do not have the confounding variable will reduce the external validity (i.e., generalizability) of the study findings.
- Block randomization, matching, stratification and multivariate statistical analysis are other ways to control for confounding and do not limit the inclusion or enrollment of study subjects; thereby not reducing external validity (generalizability).
- "A" is incorrect, yet plausible, due to the fact that it can control for confounding; however, it is a confounder-controlling-technique that does not limit patient inclusion in the study nor reduce external validity (i.e., generalizability).
- "B" is incorrect, yet plausible, due to the fact that it can control for confounding; however, it is a confounder-controlling-technique that does not limit patient inclusion in the study nor reduce external validity (i.e., generalizability).
- "D" is incorrect, yet plausible, due to the fact that it can control for confounding; however, it is a confounder-controlling-technique that does not limit patient inclusion in the study nor reduce external validity (i.e., generalizability).

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86. Your oncology colleagues approach ask you to join them in conducting the project and they have asked you what type of study design would be most appropriate to answer the research question. The question is the following: Is there a difference in exposure to cell phone- and cell tower-radiation in patients with neuroblastoma. Your colleagues anticipate obtaining the patients with neuroblastoma from their institutions' neuro-oncology clinic. Your colleagues wish to determine the differences in exposure between those with neuroblastoma and those without this disorder. They also wish to complete the research in time to meet the deadline for submission of the abstract to their favorite oncology organization's annual meeting (deadline in 6 months).

Which of the following study designs would be most appropriate for you to recommend?

A. Case-Control B Randomized Clinical C Cross-Sectional D Cohort

- Answer A
- Answer: **"B" is incorrect,** yet plausible, due to the fact that a randomized clinical trial would be unethical to force this type of exposure to patients and would be very difficult to get approved by an Institutional Review Board (IRB). Additionally, a randomized clinical trial cannot customarily be completed is a 6 month time frame. Because you already have access to the disease of interest (neuroblastoma), you want to assess the exposure status and would need to utilize an observational-style of study. A randomized clinical trial is not observation, but interventional.
- **"C" is incorrect,** yet plausible, due to the fact that a cross-sectional study is selected when you wish to observe the occurrences of an event at a given point in time. A cross-sectional study is utilized when a researcher wishes to assess prevalence of a disease or event as a slice in time (snap-shot). Due to having immediate access to cases (patients with disease) and the desire to assess for past exposure to specific types of radiation, the only matching study design would be the case-control.
- **"D" is incorrect**, yet plausible, due to the fact that cohort studies start with selecting study subjects based on their exposure status and observing them to the point of developing the disease of interest. This is completely opposite to the research question posed by your colleagues. Even though a cohort study can be conducted either prospectively (more time, and money) or retrospectively (good for short time-lines), the patient selection is not what is desired in this question. Patients already have the disease of interest (outcomes; cases) and you need to evaluate exposure (which is opposite to how a cohort study is designed (either prospective or retrospective).

87. A meta-analysis was conducted to investigate the benefits of probiotic use in the prevention and treatment of antibiotic-associated diarrhea. The study suggested that probiotics reduce the risk of antibiotic-associated diarrhea, with a relative risk of 0.58. The absolute difference in risk between the two groups was 0.07. Which one of the following is the number needed to treat (NNT) derived from the treatment group?

- A. 2.
- B. 15.
- C. 9.
- D. 20.

  - Answer B: 15.
  - The NNT is calculated as the reciprocal of the absolute difference (1/0.07), rounded to the next highest number

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88. Researchers conduct a study to determine the impact of potential risk factors on the occurrence of breast cancer. Of the techniques available to researchers useful for controlling for confounding variables, which method could ultimately reduce the external validity of their study?

A: Matching
B: Multivariate analysis
C: Restriction (C)
D: Stratification

==========

89. Your oncology colleagues would like to conduct a research project to answer a question, and they approach you to join them in conducting the project and would appreciate your input regarding the type of study design that would be most appropriate to answer the research question. The question is the following: Is there a difference in exposure to cell phone- and cell tower-radiation in patients with neuroblastoma? Your colleagues anticipate obtaining the patients with neuroblastoma from their institutions' neuro-oncology clinic. Your colleagues wish to determine the differences in exposure between those with neuroblastoma and those without this disorder. They also wish to complete the research in time to meet the deadline for submission of the abstract to their favorite oncology organization's annual meeting (deadline in 6 months). Which study design would be most appropriate for you to recommend?

A: Case-control (A)
B: Randomized clinical
C: Cross-sectional
D: Cohort

90.A study that measures the number of persons with influenza in a calendar year

A.Cohort study

B.Case control

C.Cross sectional (C)

D.Case report

==========

91.A study is being planned to investigate any link between environmental exposure to pesticides and new cases of cancer. Which of the following study designs is most appropriate?

A.Case-control study (A)

B.Case series

C.Cohort study

D.Cross-sectional survey

E.Randomized controlled trial

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92.A researcher is trying to design a study to find out the cause (or causes) of a rare disease, about which very little is known. What study design is most likely to be appropriate?

A : Geographical

B : Cross-sectional

C : Cohort

D : Intervention (D)

E : Case control

==========

93. The Women's Health Initiative trial reported a 5-year incidence of one new fracture of 8.6% (733 of 8506) in the estrogen plus medroxyprogesterone group and 11.1% (896 of 8102) in the placebo group. Which best represents the number of patients needed to treat with estrogen plus medroxyprogesterone to prevent one additional fracture?

A 2 B 4 C 25 D 40

- Answer : **11.1-8.6=2.5 100/2.5=4**

94. In a study to assess the risk of stroke, myocardial infarction, death in the first 30 days after carotid endarterectomy, individual received the experimental intervention had an event rate of 8.2 %, whereas the event rate among individuals in the control group w 3.7%. You have been asked to estimate how many people would need to be treated with this intervention for one person to experience the outcome. Which one of the following is the best interpretation of that information?

A.About 22 individuals would need to be treated with the experimental intervention for one person to be harmed by the intervention.

B.About 0.2 individuals would need to be treated with the experimental intervention for one person to benefit from the intervention.

C.About 12 individuals would need to be treated with the experimental intervention for one person to benefit from the intervention.

D.About 27 individuals would need to be treated with the experimental intervention for one person to be harmed by the intervention

- Answer: A

- **Answer A** (22 individuals) is correct because the outcome of interest is some harm, and is calculated as the inverse of the absolute risk increase. In this case, the absolute risk increase is calculated by subtracting the outcome rate in the control group (3.7%) from that in the intervention group (8.2%), giving a difference of 4.5%. Expressed as a decimal, that gives 0.045, and the inverse, or number needed to harm, is 22.2.
- **Answer B** (0.2 individuals) is incorrect because the absolute risk increase needs to be expressed in decimal terms before the inverse is taken.
- **Answer C** (12 individuals) is incorrect because this estimate is the inverse of the outcome rate in the intervention group.
- **Answer D** (27 individuals) is incorrect because this intervention is the inverse of the outcome rate in the group.

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95. Which one of the following statements is the best interpretation for an OR of 4.0?

A. The odds of having the outcome among individuals who received treatment A are 10% higher than the odds among individuals who received treatment B.

B. The odds of having the outcome are 75% lower in individuals who received treatment A than those in individuals who received treatment B.

C. The odds of having the outcome among individuals who received treatment B are 10% lower than the odds among individuals who received treatment A.

D. The odds of having the outcome are 400% higher among individuals who received treatment A than those among individuals who received treatment B.

- Answer: D

- **Answer D is correct** because the OR is an estimate of the odds of the outcome in individuals in one treatment group compared with individuals who received the other treatment. This answer represents the correct interpretation of an OR of 4.0.
- **Answer A is incorrect** because an OR of 1.1 is consistent with 10% higher odds of having the outcome among individuals who received treatment A than the odds of the outcome in individuals who received treatment B.
- **Answer B is incorrect** because this answer is consistent with an OR of 0.25.
- **Answer C is incorrect** because this is consistent with an OR of 1.1

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96. In a randomized, controlled trial, investigators assessed whether there were over all differences between two treatments. Ninety people completed the trial, divided equally between treatments. Of those who received drug A, 29 experienced the outcome, whereas of those who received drug B, 14 experienced the outcome.

Which one of the following is the best estimate of the OR for this study comparing the experience of individuals who received drug A with those who received drug B?

A. 4.0 B. 0.25 C. 1.1 D. 0.9

- Answer: A

- Answer A (OR = 4.0) is correct because the OR is estimated by cross multiplying and dividing the observed number of events, which are the four data cells of the table, not using the row or column totals at all. In this case, this calculation is od/bc = (29 x 31)/(16 x 14) = 4.01. Answer B, Answer C, and Answer D are simply incorrect calculations.

97. Relative risk and odds ratios can give an idea about the magnitude of causality between a factor and an outcome … true or false

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98. In the interpretation of a difference between odds ratio or relative risk a CI that includes one can be interpreted as not statistically …. significant true or false

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99. A new treatment for osteoarthritis has been developed and shown to be effective in animal models plus its effects in small numbers of patients appears promising. However, there are some concerns with regard to possible hepatoxicity but no cases have been observed in studies thus far. Which is the most appropriate next step in this drug's development? Available marks are shown in brackets

1) case control study [0]

2) double blind randomized placebo controlled study [0]

3) Drug development should be suspended due to the hepatoxicity [0]

4) open label study [0]

5) single blind randomized placebo controlled study [0]

- Answer 2

- This drug has completed animal trials and has been tested in human volunteers (phase 1) and has also been tried in patients (phase 2).
- Thus the next stage in its development is a phase 3 study and the best phase 3 study would be a Randomized control study.

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100. In a primary prevention study of stroke comparing a new antihypertensive with conventional antihypertensive therapy, the number of patients who had a stroke over the study period was 200 in group 1 with the new therapy (n=5200) versus 250 with conventional therapy (n=4750). Which of the following is the approximate odds ratio for the new therapy?

1) 0.25 [0] 2) 0.5 [0] 3) 0.75 [0] 4) 1 [0] 5) 1.5 [0]

- Answer 3

- An odds ratio is calculated by dividing the odds in the treated or exposed group by the odds in the control group. Studies generally try to identify factors that cause harm - those with odds ratios greater than one.
- The new therapy odds of an event is 200/5000 (patients without an event 5200-200)=0.04. Group 2's odds event rate if 250/4500 (4750-250)=0.055. The odds ratio is therefore: 0.04/0.055=0.73
  This odds ratio is less than 1, indicating an overall benefit of therapy. For calculations on Odds ratio see this article.

Or

A=200. B=250
C= 5000 d=4500
N.=5200. N..=4750
Oods Ratio=ad/cb=200*4500/5000*250=0.72
So answer 3

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101. A publication describes a new diagnostic test for myocardial infarction. You want to know what proportion of patients with a confirmed myocardial infarction will be identified by the test. Which one of the following measurements would indicate this?

1) Accuracy [0]

2) Negative predictive value [0]

3) Positive predictive value [0]

4) Sensitivity [0]

5) Specificity [0]

- The specificity of a test is the probability that a test will produce a true negative result when used on an unaffected population, whereas the sensitivity of a test is the probability that it will produce a true positive result when used on an affected population (as determined by a reference or "gold standard").
- The positive predictive value of a test is the probability that a person is affected when a positive test result is observed. The negative predictive value of a test is the probability that a person is not affected when a negative test result is observed. Accuracy is expressed through the above four parameters.

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102. A new antiplatelet agent has been proven to reduce the risk of stroke in a year from 10% in patients treated with conventional treatment to 6% in patients treated with conventional treatment plus the new agent. The cost of this new drug is £100 per month. How much extra would a hospital need to spend to prevent one stroke.

1) £1200 [0]

2) £6000 [0]

3) £18000 [0]

4) £30000 [0]

5) £100000 [0]

- Answer 4

- Comments:
  The 'Absolute Risk Reduction' is 10% - 6% = 4%. The 'Number Needed to Treat' to prevent a stroke therefore equals 100 / 4 = 25. 25 patients would need to be treated at a cost of £100/month for 12 months to prevent a stroke which gives the total cost as £30000.

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103.

Which of the following study designs can help to determine causality?

- Case Series
- Case Control Study
- Cross Sectional Study
- Randomized Clinical Control Trial

➢ Answer: RCT

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104.

. A non-inferiority trial compares the new anticoagulant (treatment A) with warfarin (standard treatment B). Which one of the following best describes what the researchers set out to prove (the alternative hypothesis)?

A. Treatment A is better than treatment B by a factor of Δ.
B. Treatment A is worse than treatment B by a factor of Δ.
C. Treatment A is not worse than treatment B by a factor of Δ.
D. Treatment A is the same as treatment B.

➢ Answer C :

- Comment: Superiority trial – a trial with the primary objective of showing that the response to the investigational product is superior to a comparative agent (active or placebo control).
- Equivalence trial – a trial with primary objective of showing that the response to two or more treatments differs by an amount which is clinically unimportant (active control).
- Non-inferiority trial – a trial with the primary objective of showing that the response to the investigational product is not clinically inferior (or not unacceptably inferior) to a

comparative agent (active or placebo control but usually active) – very common in the regulatory setting either for a new treatment or for a new label indication.

- Is the new treatment better than the control treatment that I am using now? (superiority trial)
  •If it is not better, is the new treatment as good (not unacceptably non-inferior) as the control treatment that I am using now? (non-inferiority trial)
  •Can I use the new treatment and the control treatment interchangeably? (equivalence trial) Non-inferiority and equivalence trials are usually considered when there is an active control.

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105.

You are appraising a meta-analysis of studies measuring the association between pediatric vaccinations and the development of autism. You are trying to determine whether you need to warn the parents of your pediatric patients of the risk. Which one of the following is true regarding the evaluation and application of the results of this meta-analysis?

A. If the investigators searched MEDLINE and the reference lists of all identified articles, the study would be especially susceptible to the effects of publication bias.
B. The conclusions of this meta-analysis are stronger than those in a randomized, controlled trial and should be used to guide clinical practice.
C. One disadvantage of meta-analyses is that they increase the chance for type II error.
D. One advantage of meta-analyses is that they increase the heterogeneity of the studies being analyzed, which improves the statistical analysis of the results.

- Answer : a >>>> because meta-analysis must have all data.

106.

In clinical trials, the technique in which the treatment status for experimental and control groups is concealed from study participants and/or investigators is best defined as:
Blinding
Stratification
Randomization
Washout period
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107.

A systematic review reports that its meta-analysis includes studies of the following sizes: two studies with sample sizes between 200 and 400 patients; four studies with sample sizes between 401 and 1,000 patients; one study with a sample size of 1,100 patients; and one study with a sample size of 5,200 patients. In reviewing the results for use in practice, which one of the following is the most important type of analysis to seek out?

A. A regression analysis of variables that might increase the risk of the outcome of interest
B. A sensitivity analysis and tests for heterogeneity
C. A calculation of the hazard function for the total number of patients
D. A Cox regression analysis

- Answer: Crossover trial

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108. A case-control study investigating the effect of keeping pet birds on the risk of lung cancer enrolled 200 patients presenting with lung cancer and 210 controls who were free of lung cancer. Of the 200 cases, 80 reported a history of at least 6 months' exposure to a pet bird; of the 210 controls, 70 reported such an exposure. What was the odds ratio for the development of lung cancer associated with keeping pet birds in this study?

A.1 B.8/7 C.52/45 D.6/5 E.4/3

ODD RATIO=AD/BC=80*140/70*120=4/3 SO (ANSWER>>>> E)

Risk Factor	Disease		
	+ VE	- VE	
+ VE	80 A	70 B	
- VE	120 C	140 D	